

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT
(PCT Article 18 and Rules 43 and 44)

| | | | |
|---|--|---|---|
| Applicant's or agent's file reference 16627-2PCT | FOR FURTHER ACTION | | see Form PCT/ISA/220 as well as, where applicable, item 5 below. |
| International application No. PCT/CA2004/001763 | International filing date (day/month/year) 29 September 2004 (29-09-2004) | (Earliest) Priority date (day/month/year) 29 September 2003 (29-09-2003) | |
| <p>Applicant BIOAXONE THERAPEUTIQUE INC. ET AL</p> | | | |
| <p>This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.</p> | | | |
| <p>This international search report consists of a total of <u>6</u> sheets.</p> | | | |
| <p><input checked="" type="checkbox"/> It is also accompanied by a copy of each prior art document cited in this report.</p> | | | |
| <p>1. Basis of the report</p> | | | |
| <p>a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.</p> | | | |
| <p><input type="checkbox"/> the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).</p> | | | |
| <p>b. <input checked="" type="checkbox"/> With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.</p> | | | |
| <p>2. <input checked="" type="checkbox"/> Certain claims were found unsearchable (See Box II).</p> | | | |
| <p>3. <input type="checkbox"/> Unity of invention is lacking (See Box III).</p> | | | |
| <p>4. With regard to the title.</p> | | | |
| <p><input type="checkbox"/> the text is approved as submitted by the applicant.</p> | | | |
| <p><input checked="" type="checkbox"/> the text has been established by this Authority to read as follows:</p> | | | |
| <p><i>Clostridium botulinum C3 exotransferase compositions and methods for treating tumour spreading</i></p> | | | |
| <p>5. With regard to the abstract.</p> | | | |
| <p><input checked="" type="checkbox"/> the text is approved as submitted by the applicant.</p> | | | |
| <p><input type="checkbox"/> the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.</p> | | | |
| <p>6. With regard to the drawings,</p> | | | |
| <p>a. The figure of the drawings to be published with the abstract is Figure No.</p> | | | |
| <p><input type="checkbox"/> as suggested by the applicant.</p> | | | |
| <p><input type="checkbox"/> As selected by this authority, because the applicant failed to suggest a figure.</p> | | | |
| <p><input type="checkbox"/> As selected by this Authority, because this figure better characterizes the invention.</p> | | | |
| <p>b. <input checked="" type="checkbox"/> None of the figures is to be published with the abstract.</p> | | | |

INTERNATIONAL SEARCH REPORTInternational application No.
PCT/CA2004/001763**Box No. I****Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material
 - in written format
 - in computer readable form
 - c. time of filing/furnishing
 - contained in the international application as filed
 - filed together with the international application in computer readable form
 - furnished subsequently to this Authority for the purposes of search
2. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORTInternational application No.
PCT/CA2004/001763**Box No. II****Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. Claims Nos. :
because they relate to subject matter not required to be searched by this Authority; namely:

Remark: Although claims 1-57 are directed to a method for treatment of the human or animal body, which the Authority is not obliged to search under Rule 39.1(iv) of the PCT, the search has been carried out and based on the alleged effects of the composition.
2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :
3. Claims Nos. :
because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III**Observation where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows :

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos. :
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos. :

Remark on Protest

The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2004/001763

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K 38/45, A61P 35/00, A61P 35/04, A61K 38/16, A61K 38/17, A61K 47/48, A61K 47/42

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
IPC 7 A61K 38/45, A61P 35/00, A61P 35/04, A61K 38/16, A61K 38/17, A61K 47/48, A61K 47/42

Electronic data base consulted during the international search (name of data base, and, where practicable, search terms used)

EPO-Internal, Delphion, Canadian Patent Database, Medline

Keywords: C3, transferase, ADP-ribosylation, Rho, GTPase, Clostridium, proliferation, cancer

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | | | Relevant to claim No: |
|-----------|---|-------------------------------|------------|-----------------------|
| Y | CA2342970 whole document | Mc KERRACHER, L | 2002/10/12 | 1-85 |
| Y | EP1177796 whole document, see in particular Claim 1. | MITSUBISHI PHARMA CORPORATION | 2002/02/06 | 1-85 |
| Y | VERSCHUREN, H et al. "ADP-ribosylation of Rho-proteins with botulinum C3 exoenzyme inhibits invasion and shape changes of T-lymphoma cells." European Journal of Cell Biology (1997) Vol.73, pp.182-187. whole document | | | 1-85 |
| Y | IMAMURA, F et al., "Involvement of small GTPases Rho and Rac in the invasion of rat ascites hepatoma cells." Jpn J. Cancer Res. (2000) Vol.91, pp.811-816. whole document | | | 1-85 |
| Y | YOSHIOKA, K et al., "Participation of rhop21 in serum-dependent invasion by rat ascites hepatoma cells." FEBS Letters (1995) Vol.372, pp.25-28. whole document | | | 1-85 |
| Y | US2002/0077283 A1 whole document | SESSA, WC | 2002/06/20 | 1-85 |

Further documents are listed in the continuation of Box C.

Patent family members are listed in annex.

* Special categories of cited documents :
 "A" document defining the general state of the art which is not considered to be of particular relevance
 "E" earlier application or patent but published on or after the international filing date
 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
 "O" document referring to an oral disclosure, use, exhibition or other means
 "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
 "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
 "&" document member of the same patent family

Date of the actual completion of the international-type search
10 December 2004Date of mailing of the international-type search report
22 February 2005 (22-02-2005)Name and mailing address of the ISA/CA
Commissioner of Patents
Canadian Patent Office - PCT
Ottawa/Gatineau K1A 0C9
Facsimile No. 1-819-953-9358

Authorized officer

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2004/001763

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------|
| A | VAN AELST, L and C D'SOUZA-SCHOREY "Rho GTPases and signalling networks." Genes & Development (1997) Vol.11, pp2295-2322. Whole document | 1-85 |
| A | WILDE, C et al. "Recognition of RhoA by <i>Clostridium botulinum</i> C3 Exoenzyme." Journal of Biological Chemistry (2000) Vol.275, No.22, pp.16478-16483. Whole document | 1-85 |
| A | AKTORIES, K and I JUST "Monoglucosylation of low-molecular-mass GTP-binding Rho proteins by clostridial cytotoxins." Trends in Cell Biology (1995) Vol.5, pp.441-443. Whole document | 1-85 |

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2004/001763

| Patent Document Cited in Search Report | Publication Date | Patent Family Member(s) | Publication Date |
|---|---------------------|--|--|
| CA2342970 | 12-10-2002 | CA2342970 A1 CA2362004 A1 CA2367636 A1 EP1377319 A2 JP2004532025 T T US2003103957 A1 WO02083179 A2 | 12-10-2002 12-10-2002 12-10-2002 07-01-2004 21-10-2004 05-06-2003 24-10-2002 |
| EP1177796 | 06-02-2002 | AU4144400 A CA2369560 A1 CN1362884 T T EP1177796 A1 US6794398 B1 WO0064478 A1 | 10-11-2000 02-11-2000 07-08-2002 06-02-2002 21-09-2004 02-11-2000 |
| US2002077283 | 20-06-2002 | AU9325501 A CA2421041 A1 EP1317487 A2 US2002077283 A1 US2003165510 A1 WO0220768 A2 | 22-03-2002 14-03-2002 11-06-2003 20-06-2002 04-09-2003 14-03-2002 |